

CLAIMS

1. A method of diagnosing coeliac disease, or susceptibility to coeliac disease, in an individual comprising:
 - (a) contacting a sample from the host with an agent selected from
 - (i) the epitope comprising sequence which is: SEQ ID NO:1 or 2, or an equivalent sequence from a naturally occurring homologue of the gliadin represented by SEQ ID NO:3,
 - (ii) an epitope comprising sequence comprising: SEQ ID NO:1, or an equivalent sequence from a naturally occurring homologue of the gliadin represented by SEQ ID NO:3, which epitope is an isolated oligopeptide derived from a gliadin protein,
 - (iii) an analogue of (i) or (ii) which is capable of being recognised by a T cell receptor that recognises (i) or (ii), which in the case of a peptide analogue is not more than 50 amino acids in length, or
 - (iv) a product comprising two or more agents as defined in (i), (ii) or (iii), and
 - (b) determining *in vitro* whether T cells in the sample recognise the agent; recognition by the T cells indicating that the individual has, or is susceptible to, coeliac disease.
2. Use of an agent as defined in claim 1 for the preparation of a diagnostic means for use in a method of diagnosing coeliac disease, or susceptibility to coeliac disease, in an individual, said method comprising determining whether T cells of the individual recognise the agent, recognition by the T cells indicating that the individual has, or is susceptible to, coeliac disease.
3. A method or use according to claim 1 or 2 wherein the agent is an analogue (iii) which comprises (i) or (ii) bound to (a) an HLA molecule, or (b) a fragment of an HLA molecule capable of binding (i) or (ii).

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4. A method or use according to claim 3 wherein the HLA molecule or fragment is in a complex comprising four HLA molecules or fragments of HLA molecules.
5. Use according to claim 2, 3 or 4 wherein the method comprises administering the agent to the skin of an individual and detecting the presence of inflammation at the site of administration, the detection of inflammation indicating that the T cells of the individual recognise the agent.
6. A method according to claim 1, 3 or 4 wherein the sample is blood sample.
7. A method according to claim 1, 3, 4 or 6 wherein the T cells are not restimulated in antigen specific manner *in vitro* before the said determining.
8. A method or use according to any one of the preceding claims in which the recognition of the agent by the T cells is determined by detecting the secretion of a cytokine from the T cells.
9. A method or use according to claim 8 in which the cytokine is IFN- γ .
10. A method or use according to claim 8 or claim 9 in which the cytokine is detected by allowing the cytokine to bind to an immobilised antibody specific to the cytokine and then detecting the presence of the antibody/cytokine complex.
11. A method or use according to any one of claims 1 to 7 wherein said determining is done by measuring whether the agent binds the T cell receptor.
12. A method for identifying an analogue as defined in a claim 1,3 or 4 comprising determining whether a candidate substance is recognised by a T cell receptor that recognises an epitope comprising sequence as defined in claim 1, recognition of the substance indicating that the substance is an analogue.

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13. A method of diagnosing coeliac disease, or susceptibility to coeliac disease, in an individual comprising determining the presence of an antibody that binds to an epitope of an epitope comprising sequence as defined in claim 1 in a sample from the individual, the presence of the antibody indicating that the individual has, or is susceptible to, coeliac disease.
14. An agent as defined in claim 1, optionally in association with a carrier, for use in a method of treating or preventing coeliac disease by tolerising T cells which recognise the agent.
15. An antagonist of a T cell which has a T cell receptor as defined in claim 1(iii), optionally in association with a carrier, for use in a method of treating or preventing coeliac disease by antagonising such T cells.
16. An agent as defined in claim 1 or an analogue that binds an antibody as defined in claim 13 for use in a method of treating or preventing coeliac disease in an individual by tolerising the individual to prevent the production of such an antibody.
17. A method of determining whether a composition is capable of causing coeliac disease comprising determining whether a protein capable of being modified by a transglutaminase to an oligopeptide sequence as defined in claim 1 is present in the composition, the presence of the protein indicating that the composition is capable of causing coeliac disease.
18. A method according to claim 17 wherein the said determining is done by contacting the composition with an antibody specific for the sequence which is capable of being modified to the oligopeptide sequence, binding of the antibody to a protein in the composition indicating the composition is capable of causing coeliac disease.

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19. A mutant gliadin protein whose wild-type sequence can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 1, but which mutant gliadin protein has been modified in such a way that it does not contain sequence which can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 1; or a fragment of such a mutant gliadin protein which is at least 15 amino acids long and which comprises sequence which has been modified in said way.
20. A protein that comprises a sequence which is able to bind to a T cell receptor, which T cell receptor recognises an agent as defined in claim 1, and which sequence is able to cause antagonism of a T cell that carries such a T cell receptor.
21. A method of identifying an antagonist of a T cell, which T cell recognises an agent as defined in claim 1, comprising contacting a candidate substance with the T cell and detecting whether the substance causes a decrease in the ability of the T cell to undergo an antigen specific response, the detecting of any such decrease in said ability indicating that the substance is an antagonist.
22. A kit for carrying out a method or use according to any one of claims 1 to 11 comprising an agent as defined in claim 1, 3 or 4 and a means to detect the recognition of the peptide by the T cell.
23. A kit according to claim 22 wherein the means to detect recognition comprises an antibody to IFN- γ .
24. A kit according to claim 23 wherein the antibody is immobilised on a solid support and optionally the kit also comprises a means to detect the antibody/IFN- γ complex.

25. An agent as defined in claim 1 or an antagonist as defined in claim 15.
26. A pharmaceutical composition comprising an agent or antagonist as defined in claim 25 and a pharmaceutically acceptable carrier or diluent.
27. A composition for tolerising an individual to a gliadin protein to suppress the production of a T cell or antibody response to an agent as defined in claim 1, which composition comprises an agent as defined in claim 1.
28. A composition for antagonising a T cell response to an agent as defined in claim 1, which composition comprises an antagonist as defined in claim 15.
29. Use of an agent or antagonist as defined in claim 24 or a wild type sequence as defined in claim 19 to produce an antibody specific to the agent, antagonist or wild type sequence.
30. Use of a mutation in an epitope of a gliadin protein, which epitope is as defined in claim 1, to decrease the ability of the gliadin protein to cause coeliac disease.
31. A polynucleotide that comprises a coding sequence that encodes a protein or fragment as defined in claim 19 or 20.
32. A polynucleotide according to claim 31 that additionally comprises one or more regulatory sequences operably linked to the coding sequence, which regulatory sequences are capable of securing the expression of the coding sequence in a cell.
33. A polynucleotide according to claim 32 wherein the regulatory sequence(s) allow expression of the coding sequence in a prokaryotic or mammalian cell.
34. A polynucleotide according to any one of claims 31 to 33 which is a vector or which is in the form of a vector.

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35. A cell comprising a polynucleotide as defined in any one of claims 30 to 34 or which has been transformed with such a polynucleotide.
36. A cell according to claim 35 which is a prokaryotic cell or a mammalian cell.
37. A mammal that expresses a T cell receptor as defined in claim 1.
38. Method of identifying a product which is therapeutic for coeliac disease comprising administering a candidate substance to a mammal as defined in claim 37 which has, or which is susceptible to, coeliac disease and determining whether substance prevents or treats coeliac disease in the mammal, the prevention or treatment of coeliac disease indicating that the substance is a therapeutic product.
39. A therapeutic product as identified in the method of claim 38 for use in a method of preventing or treating coeliac disease.
40. A method of diagnosing coeliac disease, or susceptibility to coeliac disease in an individual comprising administering an agent as defined in claim 1 and determining *in vivo* or *in vitro* whether T cells in the individual recognise the agent, recognition of the agent indicating that the individual has or is susceptible to coeliac disease.
41. A method of preventing or treating coeliac disease comprising administering an agent or composition as defined in claim 1 or any one of claims 26 to 28.
42. A method of preventing or treating coeliac disease comprising (a) diagnosing coeliac disease in an individual in a method as defined in claim 1 or claim 40, and (b) administering to an individual diagnosed in (a) as having, or being susceptible to, coeliac disease a therapeutic agent for preventing or treating coeliac disease.

43. A cell according to claim 35 which is a cell of a graminaceous monocotyledonous species.
44. A cell according to claim 43 which is a cell of wheat, maize, oats, rye, rice, barley, triticale, sorghum, or sugar cane.
45. A process for the production of a protein encoded by a coding sequence as defined in claim 31 which process comprises:
- (a) cultivating a cell according to any one of claims 35, 36, 43 or 44 under conditions that allow the expression of the protein; and optionally
 - (b) recovering the expressed protein.
46. A method of obtaining a transgenic plant cell comprising:
- (a) transforming a plant cell with a vector according to claim 34 to give a transgenic plant cell.
47. A method of obtaining a first-generation transgenic plant comprising:
- (b) regenerating a transgenic plant cell transformed with a vector according to claim 34 to give a transgenic plant.
48. A method of obtaining a transgenic plant seed comprising:
- (c) obtaining a transgenic seed from a transgenic plant obtainable by step (b) of claim 47.
49. A method of obtaining a transgenic progeny plant comprising obtaining a second-generation transgenic progeny plant from a first-generation transgenic

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plant obtainable by a method according to claim 47, and optionally obtaining transgenic plants of one or more further generations from the second-generation progeny plant thus obtained.

50. A method according to claim 49 comprising:

- (d) obtaining a transgenic seed from a first-generation transgenic plant obtainable by the method according to claim 48, then obtaining a second-generation transgenic progeny plant from the transgenic seed;

and/or

- (e) propagating clonally a first-generation transgenic plant obtainable by the method according to claim 47 to give a second-generation progeny plant;

and/or

- (f) crossing a first-generation transgenic plant obtainable by a method according to claim 47 with another plant to give a second-generation progeny plant;

and optionally

- (g) obtaining transgenic progeny plants of one or more further generations from the second-generation progeny plant thus obtained.

51. A transgenic plant cell, plant, plant seed or progeny plant obtainable by a method according to any one of claims 46 to 51.

52. A transgenic plant or plant seed comprising plant cells according to claim 43 or 44.

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53. A transgenic plant cell callus comprising plant cells according to claim 43 or 44 obtainable from a transgenic plant cell, first-generation plant, plant seed or progeny as defined in any one of claims 43, 44, or 46 to 50.

54. A plant or callus according to any one of claims claim 51 to 53 which is of a species as defined in claim 43 or 44.

55. A method of obtaining a crop product comprising harvesting a crop product from a plant according to any one of claims 51 to 54 and optionally further processing the harvested product.

56. A method according to claim 55 wherein the plant is a wheat plant and the harvested crop product is grain; optionally further processed into flour or another grain product.

57. A crop product obtainable by a method according to claim 55 or 56.

58. A food that comprises a protein as defined in any claim 19 or 20.

59. A food according to claim 58 in which a protein as defined in claim 19 or 20 is used instead of wild-type gliadin.